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EFFICACY OF NOVEL MAGNETIC MICROBUBBLES TARGETED TO VCAM-1 IN THE ASSESSMENT OF INFLAMMATION IN EARLY STAGE OF ATHEROSCLEROSIS

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Background: Contrast-enhanced ultrasound imaging (CEU) with site-targeted microbubbles has a potential for the detecting of inflammation in atherosclerosis that plays an important role on the stability of atherosclerotic plaque. However, the achievement of this technique in the conditions of vigorous artery flow is currently difficult due to the limited binding. We, therefore, hypothesized that a "novel" microbubbles targeted to vascular cell adhesion molecule-1 (VCAM-1) with magnetic-guided can enhance the affinity of microbubbles and be used to detect the inflammation in early stage of atherosclerosis.

Methods: The biotinylated anti-mice VCAM-1 (MBvm) or isotype antibody (MBim) was attached to the biotinylated lipid-microbubbles (LM) (or fluorescent LM) via a magnetic streptavidin bridge. The specific attachment of both agents to VCAM-1 was determined in vitro by a flow chamber at variable shear stress (1-24 dyn/cm2) without or with magnetic field (MF) and 5 min "flush". It also was determined in vivo by fluorescent microscopy and CEU imaging of the abdominal aorta at 10-min after intravenous injection of microbubbles in 24 wild-type (C57) or 24 apolipoprotein E-deficient (APOE-/-) mice on either chow diet (CD) or hypercholesgterolemic diet (HCD) for 8 weeks. MF was just used in the first 3 min after the injection. Fluorescen intensity (FI) and video intensity (VI) were measured.

Results: The attachment to the VCAM-1 was noted in MBvm but not MBim, while the firm attachment at the high shear stress (16-20dyn/cm2) was achieved only with the MF. As compared to MBim or/and without MF, FI and VI were significantly higher in the groups of MBvm or/and with MF ($P<0.05$). There were significantly differences in VI of the MBvm groups with MF (19.3±4.7, 13.2±2.7, 9.9±2.7 and 2.9±1.2 for APOE-/- mice on HCD or CD and for C57 mice on HCD or CD, respectively, $P<0.05$). As expected, the similar evidence in molecular images of abdominal aorta was noted visually.

Conclusions: The novel magnetic microbubbles targeted to the endothelial VCAM-1 could sufficiently attach to inflammatory marker at the aortic condition of high shear stress. It may be used to detect the inflammation in early stage of atherosclerosis.